CBIC Control Number
360659

DuPont Haskell Global Centers
for Health and Environmental Sciences
1090 Elkton Road, P.O. Box 50
Newark, DE 19714-0050

June 18, 2014

Via Federal Express

Document Processing Center (Mail Code 7407M)
Room 6428
Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1201 Constitution Ave., NW
Washington, DC 20004

Dear 8(e) Coordinator:

1-[2-[5-Methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl]acetyl]-4-piperidinecarbothioamide
CAS# 1003319-95-6

This letter is to inform you of the results of two oral toxicity studies in rats with the above referenced R&D test substance. To the best of our knowledge, this substance is not on the TSCA inventory.

14 Day Repeated Dose Toxicity Study
Groups of 5 male and 5 female Sprague Dawley rats received daily doses of 0, 30, 100, 300 or 1000 mg/kg/day of test substance by oral gavage for 14 consecutive days. The test substance was administered as an aqueous suspension. In-life parameters evaluated in this study included twice daily mortality checks, daily clinical signs, weekly detailed clinical examinations, twice weekly checks for body weight and food consumption. At the end of the treatment period, clinical and anatomical pathology parameters were evaluated. Test substance-related changes included increased levels of urea (24%) and BUN (23%) at 1000 mg/kg/day in males. A reduced size of the seminal vesicle was found in two male rats treated at 1000 mg/kg/day dose. Test substance related increased relative (to body) weight of liver (males: 30%, females: 15%), and kidneys (female: 7%), and decreased prostate, seminal vesicle and coagulating gland weight (33%) were noted at the 1000 mg/kg/day dose. At the dose of 300 mg/kg/day, test substance related changes were limited to increased relative (to body weight) liver weight (12%) in males. Test substance-related microscopic findings observed at 1000 mg/kg/day dose were hepatocellular hypertrophy (male: 4/5), hepatocellular single cell necrosis (male: 2/5; female: 4/5), tubular cell vacuolation in kidneys (male: 2/5, female: 5/5) and reduced fluid in seminal vesicle (male: 4/5).

90 Day Subchronic Toxicity Study
The objective of the study was to determine the subchronic toxicity of the test substance when administered by oral gavage in rats. Groups of 10 male and 10 female Sprague Dawley rats received daily oral doses of 0, 10, 50, 250, or 1000 mg/kg of the test substance for a minimum 90 consecutive days. Parameters evaluated in this study included twice daily mortality checks, daily checks for clinical signs, weekly detailed clinical examinations, weekly measurement of body weight and food consumption and ophthalmological examinations before the start and at the end of the treatment period. At the end of the treatment period, clinical and anatomical pathology parameters were evaluated. Test substance-related changes included decreased MCV (2%), MCH (3%), and reticulocyte counts (23%) at 1000 mg/kg/day dose in female rats. At 1000 mg/kg/day, test substance related increased relative (to body and brain) liver weights in both sexes and relative kidney (to body) weights in males and absolute and relative (to body and brain) kidney weights in females were observed. Histopathological findings included minimal to mild hepatocellular single cell necrosis (greater than or equal to 250 mg/kg/day in males and greater than or equal to 50 mg/kg/day in females), minimal centrilobular hepatocellular hypertrophy (1000 mg/kg/day in males and females),

minimal to moderate pigmentation in hepatocytes and Kupffer cells (1000 mg/kg/day in males and greater than or equal to 50 mg/kg/day in females), and minimal to mild tubular cell vacuolation in kidneys (greater than or equal to 250 mg/kg/day in males and females).

This information is submitted in accordance with current guidance issued by EPA indicating EPA's interpretation of Section 8(e) of the Toxic Substances Control Act or, where it is not clear that reporting criteria have been met, it is submitted as a precautionary measure and because it is information in which EPA may have an interest.

Sincerely,

S. Satheesh Anand, Ph.D., DABT
Senior Research Toxicologist
SSA/PK: jhh
(302) 366-5314

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